Comprehensive proteomics and microRNA analyses of adult neural stem cell derived exosomes after stroke

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Background: Neural stem cells (NSC) are known to facilitate healing of ischemic brain tissues. Recent studies show that NSC derived exosomes function as paracrine effectors to promote neurovascular remodeling including angiogenesis and axonal outgrowth after stroke ; nevertheless the contents of the non-stroke and post stroke NSC exosome proteome and miRNA cargo have not been determined. **Methods:** NSC derived exosomes were purified from conditional media of cultured NSCs harvested from the subventricular zone of non-ischemic and ischemic rats, respectively. Liquid chromatography mass spectrometry and miRNA array were employed to comprehensively characterize the protein and miRNA contents of NSCs and their derived exosomes after stroke. Bioinformatic analyses were performed using Ingenuity Pathway Analysis (IPA). **Results:** Exosome markers including CD63, CD9, Alix and size distribution (50-200nm) were verified with Western blot, transmission electron microscopy (TEM) and Nanosight, respectively. In total, proteomics analysis yielded 2409 and 1770 proteins identified in ischemic NSC and NSC derived exosomes, respectively. Bioinformatics analysis identified that 52, 39 and 31 proteins were related to regulating neuronal cell proliferation, migration and differentiation, respectively. In addition, 318 miRNAs were identified in ischemic NSCs with 26% of miRNAs (84 miRNAs) overlapped with parent NSCs. Gene ontology analysis showed that deregulated miRNAs were highly related to inflammation, invasion, cell proliferation, cell cycle, cell death, differentiation, etc. The top 3 upregulated mRNAs were validated in ischemic NSC-exosomes using real-time RT-PCR. **Summary/Conclusion:** Collectively, the results of our proteomic and miRNA analysis, to our knowledge, demonstrate for the first time that NSC derived exosomes contain a robust profile of protein and miRNA effectors. These data may help elucidate the function of NSC derived exosomes in stroke-induced neurogenesis, as well as potentially lead to new treatment of ischemic cerebral tissue-related diseases.

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